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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/835,976

04/16/2001

David B. Mount

1242/26/2

3961

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09/30/2004

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EXAMINER

WEGERT, SANDRA L

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 09/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/835,976

Applicant(s)

MOUNT ET AL.

Examiner

Sandra Wegert

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 June 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 and 13-103 is/are pending in the application.
- 4a) Of the above claim(s) 1-6, 14-58 and 60-100 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7-11, 13, 59 and 101-103 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 April 2001 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>7/26/04</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application, Amendments, and/or Claims

The Information Disclosure Statement, sent 26 July 2004 and the Amendment, filed 14 June 2004 have been entered. Claim 12 is canceled. Claims 101-103 have been added and read on the elected Invention. Claims 1-6, 14-58 and 60-100 were withdrawn by the examiner (12 December 2003).

Claims 7-11, 13, 59 and 101-103 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a previous Office action.

Withdrawn Objections and/or Rejections

URL's

The objection to the disclosure for containing browser-executable code is *withdrawn*. Applicants amended the Specification to remove all URL's (14 June 2004).

Claim Objections

The objection to Claims 7-13 and 59 for encompassing non-elected inventions is *withdrawn*. Applicants amended Claims 7-11, 13 and 59 to remove references to SEQ ID NO: 3-10 (14 June 2004).

The objection to Claim 59 for depending from a non-elected Claim is *withdrawn*. Applicants amended Claim 59 to remove dependencies to Claims 7, 14 or 37 (14 June 2004).

Claim Rejections - 35 USC § 112, second paragraph

The rejection of Claims 7-13 and 59 for reciting the indefinite phrase “stringent conditions,” is *withdrawn*. This rejection was made at page 10 of the previous Office Action (12 December 2003). Applicants amended independent claims to remove the phrase "stringent conditions" (14 June 2004).

Claim Rejections- 35 USC § 102

The rejection of Claims 7-13 and 59, under 35 U.S.C. 102(b), for being anticipated by Strausberg, R. (1998, Acc. No. AI313496) is *withdrawn*. Applicants amended Claims 7-11, 13 and 59 to remove reference to stringent hybridization conditions (14 June 2004). Thus, Strausberg, R. (1998, Acc. No. AI313496) does not anticipate the claims.

The rejection of Claims 7-13 and 59 under 35 U.S.C. 102(b), for being anticipated by Gu, et al (1996, Accession No. AAA99416) is *withdrawn*. Applicants amended independent claims to remove reference to "part" of the polynucleotide of SEQ ID NO: 15 (14 June 2004). Therefore, Gu, et al no longer anticipates the claims.

Maintained Objections and/or Rejections

35 USC § 112, first paragraph - scope of enablement

Claims 7-11, 12, 59 and 101-103 are rejected under 35 USC 112, first paragraph, because the specification, while being enabling for the polynucleotide of SEQ ID NO: 15, encoding a KCC3 potassium-chloride cotransporter, does not enable a polypeptide encoded by a nucleic acid

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sequence having 65-90% or more sequence identity to the nucleotide of SEQ ID NO: 15 or fragments thereof. This rejection was previously made over Claims 7-13 and 59, for sequences that possessed 75% identity to the claimed nucleic acids (12 December 2003, pages 4-8).

The instant Application does not reasonably provide enablement for various protein forms of the KCC3 transporter, wherein the protein sequence is encoded by a nucleic acid that is at least 65-90% identical to the nucleic acid of SEQ ID NO: 15, or to antigenic fragments of SEQ ID NO: 16, or to long fragments with 90% identity to SEQ ID NO: 15. The specification is not enabling for the full scope of the claimed nucleotide, wherein the nucleic acid sequence is 65-90% identical to SEQ ID NO: 15, with the assurance that enabled proteins that are functionally equivalent to SEQ ID NO: 16 can be made without undue experimentation and with the assurance that they would have the desired properties of the claimed KCC3 transporter polynucleotide. There are no examples of what specific polynucleotides fall within the range of those that would be 60-90% identical. Furthermore, since the claims do not specify a function for SEQ ID NO: 16, requiring only that the variants be *biologically active*, the claims embrace numerous polypeptides with unspecified and unknown functions, including those proteins that are structurally dissimilar but serve the same functions within a cell or organism. The specification does not disclose how to use all such variants.

As discussed in the previous Office Action, transporter family members share several recognizable structural features. However, relevant art shows that members of a class having high homology do not always share a specific and substantial functional attribute or utility, despite having structural features in common. There are many examples in which a few amino acid changes or differences in a transporter protein can inactivate it or change its substrate

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specificity (Oelmann, S., et al, 2001., J. Biol. Chem. 28(13): 26291-26300; Bisson, *et al* (1993, Crit Rev Biochem Mol Biol, 28:259-308; Liang, H., et al, 1998, Mol. Cell. Biol. 18(2): 926-935).

These examples of minor changes to transporters that resulted in a change in *function* are examples of manipulations that would render the transporter as unique. Furthermore, as discussed previously (pages 4-9, 12 December 2003), examples from the literature illustrate that it is not predictable as to which amino acids are necessary to maintain the functional characteristics of a protein.

Some of Applicant's arguments concerning the breadth of the claims center on search burden:

"Applicants respectfully submit that at a minimum, SEQ ID NOs: 7, 8, 15, and 16 can be examined together without causing an undue burden on the Patent Office" (page 22, 14 June 2004).

The other main arguments are related to whether one skilled in the art *can* make the variant nucleic acids:

"With respect to the "percent identity" element, applicants respectfully submit that one of ordinary skill in the art can construct nucleic acid molecules that fall within the scope of the claim and, upon review of the guidance provided by the present specification, can thereafter determine the percent identity between the nucleic acid sequence of the constructed molecule and SEQ ID NO: 15 [] without undue experimentation" (page 25, 14 June 2004).

Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons:

While it is true that the search burden for searching sequences other than SEQ ID NO: 15 would be too great, the scope-of-enablement rejection rests on the fact that the Applicants are enabled only to make and use *one* invention: that of SEQ ID NO: 15. As discussed previously (12 December 2003), the selectivity, sensitivity and activity of the KCC transporters are

disclosed as unique for each protein listed (see Figure 8, for example).

Furthermore, specific activities of all possible encompassed variants of the protein of SEQ ID NO: 16 and fragments comprising, are not disclosed. Applicants have not produced examples of peptide variants and fragments or a representative number of species of the claimed nucleotide variants and tested them to ensure they were functionally identical to SEQ ID NO: 16. Furthermore, since there is no discussion, or working examples disclosed in the instant case, as to what amino acids are necessary to maintain the functional characteristics of the disclosed polypeptides, the polynucleotides encoding the variants and fragments are also not useful. Although Applicants have added the phrase "biologically active" to claims in order to ensure that variant transporters have activity, applicant's claims may only encompass a transporter with the specific activity of SEQ ID NO: 16. Applicants have not made and tested all possible variants of SEQ ID NO: 16 that have the same activity of SEQ ID NO: 16. Furthermore, "biologically active" is a very broad functional requirement, encompassing all peptides, for example, that can be fed to animals (because they can be digested providing calories), or all peptides that are immunogenic (which might be true of many or most foreign proteins).

The specification does not provide a description of a process of producing and testing, nor of working examples of making, the polypeptides whose amino acid sequences deviate from the disclosed sequence (SEQ ID NO: 16) by as much as 10-40%. In addition, the predictability of the art is low with regards to the knowledge of what effects altering as much as 40% of the sequence of a polypeptide would have on the polypeptide. For this reason, undue experimentation would be required to determine a structure-function relationship for each possible polypeptide produced by the claimed nucleic acids.

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Proper analysis of the Wands factors was provided in the previous Office Action. Due to the large quantity of experimentation necessary to determine an activity or property of the claimed polynucleotide such that it can be determined how to use the polypeptides produced and to screen for activity, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing that biological activity cannot be predicted based on structural similarity, the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite particular biological activities, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

References used for a general understanding of the art:

Mount, et al, 1999, J. Biol. Chem., 274(23): 16355-16362.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

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the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

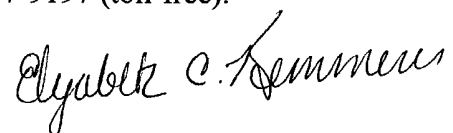
Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SLW
27 September 2004



ELIZABETH KEMMERER
PRIMARY EXAMINER